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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOWARD, ZACHARY C	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/727,195	**Applicant(s)** PEPICELLI ET AL.	
	Examiner ZACHARY C. HOWARD	**Art Unit** 1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 March 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,3,4 and 25-28*.
   Claim(s) withdrawn from consideration: *5-17*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646

Continuation of 11. does NOT place the application in condition for allowance because:

The proposed amendments filed on 3/3/08 have been entered. Applicants have canceled claims 2 and 19-24, amended claim 27 and added new claim 28. Claims 5-17 remain withdrawn from consideration as directed to a non-elected species. Claims 1, 3, 4, and 25-28 are under consideration.

All rejections of claims 2 and 19-24 are rendered moot by Applicants' cancellation of these claims.

The rejection of claim 27 under 35 U.S.C. § 103(a) at pg 9-10 of the 11/9/07 Office Action as being unpatentable over Marigo et al (U.S. Patent 6,261,786, published 7/17/01, filed 7/2/96 and claiming priority to 12/30/93; cited previously) in view of Bellusci (1997) is withdrawn in view of Applicants' amendments to claim 27.

Claims 1, 3, 4, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marigo et al (U.S. Patent 6,261,786, published 7/17/01, filed 7/2/96 and claiming priority to 12/30/93; cited previously) in view of Fujita et al (1997, cited previously). This rejection was set forth previously and maintained at pg 7-8 of the 11/9/07 Office Action.

In the 3/3/08 response, Applicants argue that Marigo et al and Fujita et al, either indvidually or in combination, fail to "teach or suggest assays in which screening is based on evaluating multiple parameters" (pg 8). Applicants argue that these two parameters are "(i) whether the agent inhibits or attenuates hedgehog signaling and (ii) whether the agent inhibits or reduces cell proliferation or growth" (pg 7-8).

Applicants' arguments have been fully considered but are not found to be persuasive. The claims do not explicity require measurement of hedgehog signaling independently from measurement of cell proliferation or growth. Instead, claim 1 recites "…determining, as compared to a control, whether the agent inhibits or attenuates hedgehog signaling and whether the agent inhibits or reduces cell proliferation or growth". Such a method broadly encompasses methods wherein determining of each is accomplished simultaneously; for example, if determining that an agent that inhibits hedgehog signaling has been inhibited inherently indicates that cell proliferation is inhibited. As set forth previously, Fujita demonstrates that an antibody to the hedgehog protein blocks proliferation of lung cancer cells, thus showing that the hedgehog signaling pathway is active in these cells and tied to proliferation of the cells (the specific teachigns of Fujita are set forth at pg 14-15 of the 5/16/07 Office Action). Fujita further teaches measuring patched gene expression in the LK-2 cells (pg 660). Thus, a determination that patched gene expression (as taught by both Marigo and Fujita) was inhibited by an agent in the LK-2 cells (taught by Fujita) would inherently also result in the determination that the agent inhibits cell proliferation.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claims contain new matter. This rejection was set forth previously for claim 27 at pg 10-11 of the 11/9/07 Office Action; new claim 28 is herewith added to the rejection.

In the 3/3/08 response, Applicants argue that claim 27 is supported by teachings in the specification, including "screening methods conducted generally in lung cells, including diseased and non-diseased cells". Applicants point to pg 15, lines 12-14 and 26-29 and page 16, lines 1-4 and page 48, lines 10-20. Applicants argue that the specification teaches that the methods could be performed with diseased cells as well as non-diseased (healthy) cells.

Applicants' arguments have been fully considered but are not found to be persuasive.

Page 15, lines 12-14 teach use of agonists and antagonists to either proliferate or inhibit proliferation of treated lung tissue. Page 15, lines 26-29 and page 16, lines 1-4 teach that compositions of the invention can be used to inhibit growth of lung-derived tissue such as treatment of hyperplastic or neoplastic conditions, including various lung cancers. Page 48, lines 10-20, discusses assay systems using "various lung cells". In none of these locations, is the term "normal lung cell" used, or a distinction made between "normal lung cells" and "abnormal lung cells".

As set forth previously, the specification does not use the phrase "normal lung cells"; nor does it describe a genus of "normal lung cells"; nor does it describe how to distinguish "normal" from "abnormal cells"; nor does it describe a method of using a specific described genus of "normal lung cells". The phrase was broadly interpreted to encompass any "lung cells" that are in their "normal" location; i.e., in vivo. Applicants have introduced the language in claim 27 that the "normal lung cells are provided in culture".

While the specification contemplates the use of cancerous cells in screening assays, there are no teachings in the specification using the specific terms "non-diseased" or "healthy" cells or that these types of cells are considered "normal" as compared to "diseased" or "cancerous" cells. Furthermore, the terms "non-diseased" or "healthy" are not necessarily equivalent to "normal". Cells in culture often undergo genetic changes that approach cancerous states as part of establishment of culture; the specification does not provide any teachings to distinguish normal cells from abnormal cells. Furthermore, any cells in culture could be considered abnormal as they are not in their native state and will undergo changes (both phenotypic and genotypic) as a result of being cultured.

New claim 28 is now included in this rejection because it depends from claim 27 and includes the same new matter.